

## PATENT ABSTRACTS OF JAPAN

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## (54) BIOMEDICAL CEMENT

## (57)Abstract:

PURPOSE: To provide biomedical cement of which hardening speed is high and strength can be kept for a long time, by using inorganic composition of which  $\text{CaO}+\text{P}_2\text{O}_5$ ,  $\text{B}_2\text{O}_3$  and other components are in specific rates and using phosphoric acid-ammonium phosphate water solution as hardening liquid.

CONSTITUTION: Powder obtained by pulverizing solid, which an inorganic component with a composition ratio of  $\text{CaO}+\text{P}_2\text{O}_5$ , 60-80mol%,  $\text{B}_2\text{O}_3$  10-30mol% and other inorganic components 0-10-mol% is heated up to 1000° C-1300° C to be melted then cooled, and hardening liquid composed of phosphoric acid and ammonium phosphate water solution are used to make biomedical cement. The  $\text{CaO}/\text{P}$  ratio of the powder is to be 1.5-3.0, and the hardening liquid is to contain phosphoric acid 20-50wt.% and ammonium phosphate 10-30wt.%. Biomedical cement with high strength and high biomedical affinity can be obtained by this method.

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CLAIMS

[Claim(s)]

[Claim 1](A)  $\text{CaO} + \text{P}_2\text{O}_5$  60-80-mol% and  $\text{B}_2\text{O}_3$  10-30-mol%, Cement for living bodies characterized by powder produced by grinding a solid produced by cooling after warming and carrying out melting of the mineral constituent which has other 0-10 mol of mineral constituent% of composition ratio to 1000 \*\* - 1300 \*\*, and sclerosing solution which consists of a (B) phosphoric acid-ammonium phosphate salt water solution.

[Claim 2]The cement for living bodies according to claim 1 whose Ca/P ratios of powder of (A) are 1.5-3.0.

[Claim 3]The cement for living bodies according to claim 1 or 2 in which sclerosing solution of (B) contains 20 to 50 % of the weight of phosphoric acid, and 10 to 30 % of the weight of ammonium phosphate salts.

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## DETAILED DESCRIPTION

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[Detailed Description of the Invention]

[0001]

[Industrial Application]This invention relates to cement for living bodies. The cement for living bodies provided by this invention can be used as the filler or reinforcing member of a bony lacking part or a cavity part. After making arbitrary shape solidify itself, it can be used as support, such as bone substitution material or a cell, and bacteria.

[0002]

[Description of the Prior Art]When a bony deficit arises from the former in medical fields, such as dentistry, oral surgery, orthopedics, and surgery, the bone grafting by the private bone or a bone of the same kind has been performed as a method of treating this. However, since there are a quantitative problem that it is difficult to secure a private bone and other \*\*\* in large quantities, and a mental and corporal problem of forcing a bone donor pain in such bone grafting, there is a limit, and development of an artificial bone and an artificial bone filler came to be performed briskly. Although there were metal and ceramics as such an artificial bone and an artificial bone filler, especially, a calcium phosphate system compound attracts attention as a raw material with the character coupled directly with a bone, and came to be put in practical use.

[0003]However, although excelled in biocompatibility, since processing of shape is not easy, though the bulking agent made from ceramics can be prepared for beforehand [ metaphor ], it is dramatically difficult [ bulking agent / preparing in the shape of a filling portion is difficult for it, and ] to amend shape according to the affected part during an operation. Although being filled up with hydroxyapatite or the powder of a calcium phosphate system like phosphoric acid TORIKARUSHIUMU is also performed, since such powder does not have hardenability, it does not have the intensity after restoration, and it may leak out from the affected part with which it filled up, and a limit is in the situation which can be used. Since it being precisely filled up to the details of a cavity part and after--restoration cement will solidify if it is this point hardenability cement, it does not move and leak out, and intensity also has the advantage that sufficient thing is obtained, and cement for living bodies, such as a calcium phosphate system constituent of hydration hardenability, is developed.

[0004]However, the ingredient in powder mixture is eluted, and since what carries out hydration hardening uses the mechanism which a crystal becomes entangled and hardens when it changes to the substance of insoluble in water nature and is recrystallized, it will take 30 minutes or more for a cure rate to solidify late generally. When come and there is nothing without being able to perform a tangle of a crystal enough, or when a crystal's own intensity is low, application is difficult for the part to which the intensity after hardening becomes very low, and a load requires it.

[0005]In addition, although the thing which mixes the solution of an ammonium phosphate salt or polycarboxylic acid with the powder of the living body activity glass ceramics which deposited the calcium silicate and the calcium phosphate system crystal, and it is made to solidify is also developed. Usually, since  $\text{SiO}_2$  contains 30 to 70% of the weight in glass--ceramics powder, the quantity of calcium which is a living body affinity ingredient, or phosphorus decreases, and

substitution to a private bone is no longer performed enough. Since what uses polycarboxylic acid for sclerosing solution used the metallic component in glass, and the chelate bond of polycarboxylic acid, cure time was early, but there was a problem that we were anxious about exfoliation of cement by degradation by the temporality of a polycarboxylic acid portion and omission.

[0006]

[Problem(s) to be Solved by the Invention] This invention is made in view of this actual condition, a cure rate is quick and intensity makes it SUBJECT to provide the cement for living bodies outstanding as a packing material maintained at a long period of time.

[0007]

[Means for Solving the Problem] this invention person has found out mainly generating beta-TCP 60% of the weight or more in a composition component, if it cools after fusing a mixture of specific composition ratio at 1000-1300 \*\*, but. As a result of advancing research, when this constituent was powdered and addition mixing of the phosphoric acid-ammonium phosphate salt water solution was carried out, it hardened in 2 to 10 minutes, found out that considerable intensity is obtained from early stages of hardening, and that the last attainment intensity was maintained for a long period of time, and resulted in this invention.

[0008] Composition ratio of a raw material this invention Namely,  $\text{CaO} + \text{P}_2\text{O}_5$  60-80-mol%, Cement for living bodies which is  $\text{B}_2\text{O}_3$  10-30-mol % and 0-10 mol of other mineral constituent %, and is characterized by a Ca/P ratio's using as a cement component powder of an inorganic composition which are 1.5-3.0, and using a phosphoric acid-ammonium phosphate salt water solution as sclerosing solution is provided.

[0009] This invention is explained in detail below.

[0010] In this invention, composition ratio of a raw material is  $\text{CaO} + \text{P}_2\text{O}_5$  60-80-mol % and 0-10 mol of other mineral constituent %, and a Ca/P ratio uses powder of an inorganic composition which are 1.5-3.0 as a cement component. [ % and  $\text{B}_2\text{O}_3$  10-30 mol ] Powder of such an inorganic composition can be obtained by a method indicated by the Japanese-Patent-Application-No. No. 171181 [ four to ] gazette, For example, calcium salt, phosphate, a calcium phosphate salt, way acid, way acid chloride, Oxidation boron etc. are mixed so that the above-mentioned composition range and composition ratio may be satisfied eventually, and after warming and carrying out melting to 1000-1300 \*\* with platina crucible etc., it is obtained by carrying out disintegration of the solid obtained by cooling with grinders, such as a ball mill.

[0011] Ammonium phosphate salt of phosphoric acid is [ concentration of sclerosing solution / 10 to 30% of the weight of a range ] preferred 20 to 50% of the weight. If intensity runs short if phosphoric acid is less than 20 % of the weight, and cure time also becomes long too much and exceeds 50 % of the weight, cure time passes early and is not practical. Since a hardening reaction will be early seen [ an exothermic phenomenon ] if quantity of an ammonium phosphate salt is less than 10%, if 30 % of the weight is exceeded undesirably [ so ], it will be hard to dissolve, and also delay of a hardening reaction comes to be conspicuous.

[0012] As a raw material of sclerosing solution, orthophosphoric acid, ammonium dihydrogen phosphate, diammonium hydrogen phosphate, etc. can use it conveniently.

[0013] By mixing with a phosphoric acid-ammonium phosphate salt water solution, it hardens in a short time for 2 minutes - 10 minutes, moreover, compressive strength 1 hour after hardening reaches before and after 300 Kgf/cm<sup>2</sup>, and an inorganic composition of the above-mentioned presentation gives cement whose compressive strength is higher than early stages of hardening.

In 8 hours, compressive strength increases this cement even before and after 700 - 800 kg/cm<sup>2</sup>, and even if this figure is immersed in a false living body solution for one month, it does not fall.

[0014] As for this cement powder, it is preferred to grind to particle diameter of 200 or less meshes. It is better to avoid, since combination between particles will become weak and will cause a strong fall, if particle diameter is larger than 200 meshes.

[0015] As for the mixing ratio of cement powder and sclerosing solution, it is preferred to mix 0.2-0.6 ml of sclerosing solution to the cement powder 1g. It is difficult to mix with cement

powder enough, and if 0.6 ml is exceeded, there will be too much sclerosing solution, contact between powder particles will become less enough [ 0.2 ml or less ] as, and intensity after hardening will fall by it.

[0016](Example of manufacture of cement powder for living bodies) So that it may become the presentation of Table 1 Calcium carbonate, Superfluous ethanol was put into back alumina crucible transpired on a water bath, and what could mix orthophosphoric acid and way acid, could add ethanol, and was stirred was warmed to 1300 \*\* with an electric furnace at the rate of 10 \*\* / min. After fusing at this temperature for 4 hours, it cooled radiationally automatically within a furnace and a white solid was obtained. After grinding this white constituent to about one mm square using a mortar made from alumina, and a pestle made from alumina, it ground by the Fritsch planetary ball mill for 20 minutes, and was considered as impalpable powder of 200 or less meshes, and cement powder of the examples 1-4 of manufacture was obtained.

[0017]

[Table 1]

	製造例 1	製造例 2	製造例 3	製造例 4
CaO	64.00	61.50	63.75	63.75
P <sub>2</sub> O <sub>5</sub>	16.00	16.50	21.25	21.25
B <sub>2</sub> O <sub>3</sub>	20.00	20.00	5.00	5.00
SiO <sub>2</sub>	--	--	7.50	2.50
Al <sub>2</sub> O <sub>3</sub>	--	--	2.50	7.50

\*表示はmol%

[0018](Example of manufacture of sclerosing solution) Orthophosphoric acid and 2 hydrogen sodium phosphate was used as solution, and sclerosing solution of the examples 5-8 of manufacture was obtained so that it might become the presentation of Table 2.

[0019]

[Table 2]

	製造例 5	製造例 6	製造例 7	製造例 8
オルト燐酸	50	40	35	30
燐酸二水素アンモニウム	10	--	15	15
燐酸水素二アンモニウム	--	10	--	5
蒸留水	40	50	50	50

\*表示は重量%

[0020]

[Example]An example explains this invention in detail below.

[0021]The cement powder 20g of the example 1 of example 1. manufacture and 5 ml of sclerosing solution of the example 5 of manufacture were mixed, and the 1x1x2-cm metallic mold made from brass was filled up.

[0022]The cement powder 20g of the example 2 of example 2. manufacture and 5 ml of sclerosing solution of the example 6 of manufacture were mixed, and the 1x1x2-cm metallic mold made from brass was filled up.

[0023]The cement powder 20g of the example 3 of example 3. manufacture and 7.5 ml of sclerosing solution of the example 7 of manufacture were mixed, and the 1x1x2-cm metallic mold made from brass was filled up.

[0024]The cement powder 20g of the example 4 of example 4. manufacture and 10 ml of sclerosing solution of the example 8 of manufacture were mixed, and the 1x1x2-cm metallic mold made from brass was filled up.

[0025]Cure time made cure time time [ to have dropped the needle of 300 g in weight, and cross-section area / of 1 mm / <sup>2</sup> to the kneaded material with which the metallic mold was filled up, and ] no longer attaching to it.

[0026]Compressive strength took out packing hardened 2 hours after metallic mold restoration and 8 hours afterward, and measured it with the compression testing machine by a cage ene tech company. Packing taken out 8 hours afterward was immersed in 199 liquid media for three months, and compressive strength was measured similarly.

[0027]Identification of the crystal phase of what ground powder and the hardened cement before mixing with sclerosing solution, and a fixed quantity of the crystal were measured with the X-ray diffractometer by JEOL Co., Ltd. The above result was shown in Table 3.

[0028]

[Table 3]

	実施例 1	実施例 2	実施例 3	実施例 4
硬化時間	2分	4分	5分	7分
2時間後の圧縮強度	280Kgf/cm <sup>2</sup>	315Kgf/cm <sup>2</sup>	345Kgf/cm <sup>2</sup>	320Kgf/cm <sup>2</sup>
8時間後の圧縮強度	720Kgf/cm <sup>2</sup>	760Kgf/cm <sup>2</sup>	880Kgf/cm <sup>2</sup>	835Kgf/cm <sup>2</sup>
3ヶ月浸漬後の圧縮強度	715Kgf/cm <sup>2</sup>	760Kgf/cm <sup>2</sup>	820Kgf/cm <sup>2</sup>	830Kgf/cm <sup>2</sup>
セメント粉末の結晶相	$\beta$ -TCP	$\beta$ -TCP	$\beta$ -TCP	$\beta$ -TCP
セメント粉末中の結晶量	79.6	77.4	67.6	68.3
硬化体の結晶相	$\beta$ -TCP	$\beta$ -TCP	$\beta$ -TCP	$\beta$ -TCP
硬化体中の結晶量	78.8	76.5	66.9	68.2

\*結晶量の定置値は重量%

[0029]As shown in the result of Table 3, cement for living bodies of this invention carries out self-coagulation hardening at an early stage, and its compressive strength is high from the early stages of hardening. Even after being immersed in false living body liquid for three months, the fall of compressive strength is not accepted but holds stable compressive strength. It was proved that after the amount of crystals of high  $\beta$ -TCP of compatibility to a living body and a hardening reaction hardly changed etc.

[0030]

[Effect of the Invention]According to this invention, cement for living bodies with high biocompatibility with a quick cure rate and high and intensity can be provided.

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TECHNICAL FIELD

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[Industrial Application]This invention relates to cement for living bodies. The cement for living bodies provided by this invention can be used as the filler or reinforcing member of a bony lacking part or a cavity part. After making arbitrary shape solidify itself, it can be used as support, such as bone substitution material or a cell, and bacteria.

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PRIOR ART

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[Description of the Prior Art]When a bony deficit arises from the former in medical fields, such as dentistry, oral surgery, orthopedics, and surgery, the bone grafting by the private bone or a bone of the same kind has been performed as a method of treating this. However, since there are a quantitative problem that it is difficult to secure a private bone and other \*\*\*\* in large quantities, and a mental and corporal problem of forcing a bone donor pain in such bone grafting, there is a limit, and development of an artificial bone and an artificial bone filler came to be performed briskly. Although there were metal and ceramics as such an artificial bone and an artificial bone filler, especially, a calcium phosphate system compound attracts attention as a raw material with the character coupled directly with a bone, and came to be put in practical use.

[0003]However, although excelled in biocompatibility, since processing of shape is not easy, though the bulking agent made from ceramics can be prepared for beforehand [ metaphor ], it is dramatically difficult [ bulking agent / preparing in the shape of a filling portion is difficult for it, and ] to amend shape according to the affected part during an operation. Although being filled up with hydroxyapatite or the powder of a calcium phosphate system like phosphoric acid TORIKARUSHIUMU is also performed, since such powder does not have hardenability, it does not have the intensity after restoration, and it may leak out from the affected part with which it filled up, and a limit is in the situation which can be used. Since it being precisely filled up to the details of a cavity part and after-restoration cement will solidify if it is this point hardenability cement, it does not move and leak out, and intensity also has the advantage that sufficient thing is obtained, and cement for living bodies, such as a calcium phosphate system constituent of hydration hardenability, is developed.

[0004]However, the ingredient in powder mixture is eluted, and since what carries out hydration hardening uses the mechanism which a crystal becomes entangled and hardens when it changes to the substance of insoluble in water nature and is recrystallized, it will take 30 minutes or more for a cure rate to solidify late generally. When come and there is nothing without being able to perform a tangle of a crystal enough, or when a crystal's own intensity is low, application is difficult for the part to which the intensity after hardening becomes very low, and a load requires it.

[0005]In addition, although the thing which mixes the solution of an ammonium phosphate salt or polycarboxylic acid with the powder of the living body activity glass ceramics which deposited the calcium silicate and the calcium phosphate system crystal, and it is made to solidify is also developed. Usually, since  $\text{SiO}_2$  contains 30 to 70% of the weight in glass-ceramics powder, the quantity of calcium which is a living body affinity ingredient, or phosphorus decreases, and substitution to a private bone is no longer performed enough. Since what uses polycarboxylic acid for sclerosing solution used the metallic component in glass, and the chelate bond of polycarboxylic acid, cure time was early, but there was a problem that we were anxious about exfoliation of cement by degradation by the temporality of a polycarboxylic acid portion and omission.



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EFFECT OF THE INVENTION

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TECHNICAL PROBLEM

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MEANS

[Means for Solving the Problem]this invention person has found out mainly generating beta-TCP 60% of the weight or more in a composition component, if it cools after fusing a mixture of specific composition ratio at 1000-1300 \*\*, but. As a result of advancing research, when this constituent was powdered and addition mixing of the phosphoric acid-ammonium phosphate salt water solution was carried out, it hardened in 2 to 10 minutes, found out that considerable intensity is obtained from early stages of hardening, and that the last attainment intensity was maintained for a long period of time, and resulted in this invention.

[0008]Composition ratio of a raw material this invention Namely,  $\text{CaO} + \text{P}_2\text{O}_5$  60-80-mol%, Cement for living bodies which is  $\text{B}_2\text{O}_3$  10-30-mol % and 0-10 mol of other mineral constituent %, and is characterized by a Ca/P ratio's using as a cement component powder of an inorganic composition which are 1.5-3.0, and using a phosphoric acid-ammonium phosphate salt water solution as sclerosing solution is provided.

[0009]This invention is explained in detail below.

[0010]In this invention, composition ratio of a raw material is  $\text{CaO} + \text{P}_2\text{O}_5$  60-80-mol % and 0-10 mol of other mineral constituent %, and a Ca/P ratio uses powder of an inorganic composition which are 1.5-3.0 as a cement component. [ % and  $\text{B}_2\text{O}_3$  10-30 mol ] Powder of such an inorganic composition can be obtained by a method indicated by the Japanese-Patent-Application-No. No. 171181 [ four to ] gazette, For example, calcium salt, phosphate, a calcium phosphate salt, way acid, way acid chloride, Oxidation boron etc. are mixed so that the above-mentioned composition range and composition ratio may be satisfied eventually, and after warming and carrying out melting to 1000-1300 \*\* with platina crucible etc., it is obtained by carrying out disintegration of the solid obtained by cooling with grinders, such as a ball mill.

[0011]Ammonium phosphate salt of phosphoric acid is [ concentration of sclerosing solution / 10 to 30% of the weight of a range ] preferred 20 to 50% of the weight. If intensity runs short if phosphoric acid is less than 20 % of the weight, and cure time also becomes long too much and exceeds 50 % of the weight, cure time passes early and is not practical. Since a hardening reaction will be early seen [ an exothermic phenomenon ] if quantity of an ammonium phosphate salt is less than 10%, if 30 % of the weight is exceeded undesirably [ so ], it will be hard to dissolve, and also delay of a hardening reaction comes to be conspicuous.

[0012]As a raw material of sclerosing solution, orthophosphoric acid, ammonium dihydrogen phosphate, diammonium hydrogen phosphate, etc. can use it conveniently.

[0013]By mixing with a phosphoric acid-ammonium phosphate salt water solution, it hardens in a short time for 2 minutes - 10 minutes, moreover, compressive strength 1 hour after hardening reaches before and after 300 Kgf/cm<sup>2</sup>, and an inorganic composition of the above-mentioned presentation gives cement whose compressive strength is higher than early stages of hardening. In 8 hours, compressive strength increases this cement even before and after 700 - 800 kg/cm<sup>2</sup>, and even if this figure is immersed in a false living body solution for one month, it does not fall.

[0014]As for this cement powder, it is preferred to grind to particle diameter of 200 or less meshes. It is better to avoid, since combination between particles will become weak and will

cause a strong fall, if particle diameter is larger than 200 meshes.

[0015]As for the mixing ratio of cement powder and sclerosing solution, it is preferred to mix 0.2-0.6 ml of sclerosing solution to the cement powder 1g. It is difficult to mix with cement powder enough, and if 0.6 ml is exceeded, there will be too much sclerosing solution, contact between powder particles will become less enough [ 0.2 ml or less ] as, and intensity after hardening will fall by it.

[0016](Example of manufacture of cement powder for living bodies) So that it may become the presentation of Table 1 Calcium carbonate, Superfluous ethanol was put into back alumina crucible transpired on a water bath, and what could mix orthophosphoric acid and way acid, could add ethanol, and was stirred was warmed to 1300 \*\* with an electric furnace at the rate of 10 \*\* / min. After fusing at this temperature for 4 hours, it cooled radiationally automatically within a furnace and a white solid was obtained. After grinding this white constituent to about one mm square using a mortar made from alumina, and a pestle made from alumina, it ground by the Fritsch planetary ball mill for 20 minutes, and was considered as impalpable powder of 200 or less meshes, and cement powder of the examples 1-4 of manufacture was obtained.

[0017]

[Table 1]

	製造例 1	製造例 2	製造例 3	製造例 4
CaO	84.00	81.50	83.75	83.75
P <sub>2</sub> O <sub>5</sub>	18.00	18.50	21.25	21.25
B <sub>2</sub> O <sub>3</sub>	20.00	20.00	5.00	5.00
SiO <sub>2</sub>	--	--	7.50	2.50
Al <sub>2</sub> O <sub>3</sub>	--	--	2.50	7.50

\*表示はmo1%

[0018](Example of manufacture of sclerosing solution) Orthophosphoric acid and 2 hydrogen sodium phosphate was used as solution, and sclerosing solution of the examples 5-8 of manufacture was obtained so that it might become the presentation of Table 2.

[0019]

[Table 2]

	製造例 5	製造例 6	製造例 7	製造例 8
オルト磷酸	50	40	35	30
磷酸二水素アンモニウム	10	--	15	15
磷酸水素アンモニウム	--	10	--	5
蒸留水	40	50	50	50

\*表示は重量%

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## EXAMPLE

[Example]An example explains this invention in detail below.

[0021]The cement powder 20g of the example 1 of example 1. manufacture and 5 ml of sclerosing solution of the example 5 of manufacture were mixed, and the 1x1x2-cm metallic mold made from brass was filled up.

[0022]The cement powder 20g of the example 2 of example 2. manufacture and 5 ml of sclerosing solution of the example 6 of manufacture were mixed, and the 1x1x2-cm metallic mold made from brass was filled up.

[0023]The cement powder 20g of the example 3 of example 3. manufacture and 7.5 ml of sclerosing solution of the example 7 of manufacture were mixed, and the 1x1x2-cm metallic mold made from brass was filled up.

[0024]The cement powder 20g of the example 4 of example 4. manufacture and 10 ml of sclerosing solution of the example 8 of manufacture were mixed, and the 1x1x2-cm metallic mold made from brass was filled up.

[0025]Cure time made cure time time [ to have dropped the needle of 300 g in weight, and cross-section area / of 1 mm / <sup>2</sup> to the kneaded material with which the metallic mold was filled up, and ] no longer attaching to it.

[0026]Compressive strength took out packing hardened 2 hours after metallic mold restoration and 8 hours afterward, and measured it with the compression testing machine by a cage ene tech company. Packing taken out 8 hours afterward was immersed in 199 liquid media for three months, and compressive strength was measured similarly.

[0027]Identification of the crystal phase of what ground powder and the hardened cement before mixing with sclerosing solution, and a fixed quantity of the crystal were measured with the X-ray diffractometer by JEOL Co., Ltd. The above result was shown in Table 3.

[0028]

[Table 3]

	実施例 1	実施例 2	実施例 3	実施例 4
硬化時間	2分	4分	5分	7分
2時間後の圧縮強度	280kgf/cm <sup>2</sup>	315kgf/cm <sup>2</sup>	345kgf/cm <sup>2</sup>	320kgf/cm <sup>2</sup>
8時間後の圧縮強度	720kgf/cm <sup>2</sup>	780kgf/cm <sup>2</sup>	880kgf/cm <sup>2</sup>	835kgf/cm <sup>2</sup>
3ヶ月浸漬後の圧縮強度	715kgf/cm <sup>2</sup>	780kgf/cm <sup>2</sup>	820kgf/cm <sup>2</sup>	830kgf/cm <sup>2</sup>
セメント粉末の結晶相	β-TCP	β-TCP	β-TCP	β-TCP
セメント粉末中の結晶量	79.6	77.4	67.6	68.3
硬化体の結晶相	β-TCP	β-TCP	β-TCP	β-TCP
硬化体中の結晶量	78.8	76.5	66.9	68.2

\*結晶量の測定値は重量%

[0029]As shown in the result of Table 3, cement for living bodies of this invention carries out self-coagulation hardening at an early stage, and its compressive strength is high from the early stages of hardening. Even after being immersed in false living body liquid for three months, the fall of compressive strength is not accepted but holds stable compressive strength. It was proved that after the amount of crystals of high beta-TCP of compatibility to a living body and a hardening reaction hardly changed etc.

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[Translation done.]

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(54) 【発明の名称】 生体用セメント

(57) 【要約】

【目的】 硬化速度が速く、強度が高く且つ生体親和性の高い生体用セメントを提供する。

【構成】  $\text{CaO} + \text{P}_2\text{O}_5$  60～80m o l %、 $\text{B}_2\text{O}_3$  10～30m o l %、他の無機成分 0～10m o l % の組成比を有する粉末と、磷酸－磷酸アンモニウム塩水溶液とからなる。



## 【特許請求の範囲】

【請求項1】 (A)  $\text{CaO} + \text{P}_2\text{O}_5$  60～80mol %、 $\text{B}_2\text{O}_3$  10～30mol %、他の無機成分0～10mol %の組成比を有する無機成分を、1000℃～1300℃まで加温して溶融させた後、冷却して得られる固体を粉砕して得られる粉末と、(B) 燐酸-燐酸アンモニウム塩水溶液からなる硬化液を特徴とする生体用セメント。

【請求項2】 (A) の粉末のCa/P比が1.5～3.0である請求項1に記載の生体用セメント。

【請求項3】 (B) の硬化液が燐酸20～50重量%、燐酸アンモニウム塩10～30重量%を含む請求項1又は2に記載の生体用セメント。

## 【発明の詳細な説明】

【0001】

【産業上の利用分野】本発明は生体用セメントに関する。本発明により提供される生体用セメントは骨の欠損部や空隙部の充填材又は補強材として使用できる。また、それ自身を任意の形状に固化させた後、骨置換材或いは細胞や細菌等の担持体として使用する事が出来る。

【0002】

【従来の技術】従来から歯科、口腔外科、整形外科、外科等の医療分野で骨の欠損が生じた場合、これを治療する方法として自家骨や同種骨による骨移植が行われてきた。しかしながら、このような骨移植には自家骨や他家骨を大量に確保する事が困難であるという量的な問題や、骨提供者に苦痛を強いるという精神的、肉体的な問題があるため限界があり、人工骨及び人工骨充填材の開発が盛んに行われるようになった。このような人工骨及び人工骨充填材としては金属やセラミックスがあるが、なかでも燐酸カルシウム系化合物は骨と直接結合する性質がある素材として注目され、実用化されるようになった。

【0003】しかしながら、セラミックス製の充填剤は生体親和性には優れているが、形状の加工が容易ではないため、充填部の形状に整える事が難しく、例え事前に準備可能であったとしても施術中に患部に合わせて形状を補正する事が非常に困難である。ハイドロキシアパタイトや燐酸トリカルシウムのような燐酸カルシウム系の粉末を充填することも行われているが、このような粉末は硬化性を持たないため充填後の強度がなく、また充填された患部から漏出する事があり、使用出来る状況には限界がある。この点硬化性セメントならば空隙部の細部まで緻密に充填できること、充填後セメントが固化するので移動、漏出する事が無く、強度も十分なものが得られるという利点があり、水和硬化性の燐酸カルシウム系組成物等の生体用セメントが開発されている。

【0004】ところが、水和硬化させるものは、混合粉末中の成分が溶出し、水不溶性の物質に変化して再結晶する際に、結晶が絡み合って硬化する機構を利用する

為、一般に硬化速度が遅く凝固するのに30分以上を要してしまう。また、結晶の絡み合いが十分出来ない場合や結晶自身の強度が低い場合には、硬化後の強度が極めて低くなり、加重のかかる部位には適用が難しい。

【0005】この他珪酸カルシウムや燐酸カルシウム系結晶を析出させた生体活性結晶化ガラスの粉末に燐酸アンモニウム塩やポリカルボン酸の水溶液を混和して固化させるものも開発されているが、通常結晶化ガラス粉末中に $\text{SiO}_2$ が30～70重量%含有されるので、生体親和成分であるカルシウムや燐の量が減少してしまい、自家骨への置換が十分行われなくなる。又、ポリカルボン酸を硬化液に用いるものはガラス中の金属成分とポリカルボン酸のキレート結合を利用しているので、硬化時間は早いですが、ポリカルボン酸部分の経時での劣化によるセメントの剥離、脱落が懸念されるという問題があった。

【0006】

【発明が解決しようとする課題】本発明は斯かる実状に鑑みてなされたものであって、硬化速度が速く且つ強度が長期に維持される、充填材料として優れた生体用セメントを提供することを課題とする。

【0007】

【課題を解決するための手段】本発明者は、特定の組成比の混合物を1000～1300℃で溶融した後冷却すると、組成成分中に主として $\beta$ -TCPを60重量%以上生成する事を見いだしているが、更に研究を進めた結果、該組成物を粉末とし、燐酸-燐酸アンモニウム塩水溶液を添加混合してやると、2～10分で硬化し、硬化初期から相当の強度が得られる事、また最終到達強度が長期間維持される事を見だし、本発明に至った。

【0008】すなわち本発明は、原料の組成比が、 $\text{CaO} + \text{P}_2\text{O}_5$  60～80mol %、 $\text{B}_2\text{O}_3$  10～30mol %、他の無機成分0～10mol %で且つCa/P比が1.5～3.0である無機組成物の粉末をセメント成分とし、硬化液として燐酸-燐酸アンモニウム塩水溶液を用いる事を特徴とする生体用セメントを提供する。

【0009】以下本発明を詳細に説明する。

【0010】本発明では、原料の組成比が、 $\text{CaO} + \text{P}_2\text{O}_5$  60～80mol %、 $\text{B}_2\text{O}_3$  10～30mol %、他の無機成分0～10mol %で且つCa/P比が1.5～3.0である無機組成物の粉末をセメント成分として用いる。このような無機組成物の粉末は特願平4-171181号公報に開示された方法で得る事が出来、例えばカルシウム塩、燐酸塩、燐酸カルシウム塩、ほう酸、ほう酸塩、酸化ほう素等を最終的に上記組成範囲及び組成比を満足するように混合し、プラチナ坩堝等で1000～1300℃まで加温して溶融させた後、冷却する事により得られた固体をボールミル等の粉砕機で粉末化する事により得られる。

【0011】硬化液の濃度は燐酸が20～50重量%、燐酸アンモニウム塩が10～30重量%の範囲が好ましい。燐酸が20重量%未満だと強度が不足し硬化時間も長くなりすぎ、50重量%を越えると、硬化時間が早くなりすぎ、実用的ではない。燐酸アンモニウム塩の量が10%未満だと硬化反応が早く、発熱現象が見られるので余り好ましくなく、30重量%を越えると溶解しがたい上、硬化反応の遅延が目立つようになる。

【0012】硬化液の原料としては、オルト燐酸、燐酸二水素アンモニウム、燐酸水素二アンモニウム等が好適に使用できる。

【0013】上記組成の無機組成物は燐酸-燐酸アンモニウム塩水溶液と混和する事により2分～10分の短時間で硬化し、しかも硬化1時間後の圧縮強度が300Kgf/cm<sup>2</sup>前後に達し、硬化初期より圧縮強度の高いセメントを与える。更にはこのセメントは8時間後には700～800Kgf/cm<sup>2</sup>前後にまで圧縮強度が増加し、この数値は疑似生体溶液に1ヶ月浸漬しても低下しない。

【0014】このセメント粉末は200メッシュ以下の粒径に粉砕する事が好ましい。200メッシュより粒径が大きいと、粒子間の結合が弱くなり、強度の低下を招くので避けた方がよい。

【0015】セメント粉末と硬化液との混合比率はセメント粉末1gに対し硬化液を0.2～0.6ml混合する事が好ましい。0.2ml以下ではセメント粉末と十分混和する事が難しく、又0.6mlを越えると硬化液

が多すぎて粉末粒子間の接触が十分でなくなり、硬化後の強度が低下する。

【0016】(生体用セメント粉末の製造例)表1の組成となるように、炭酸カルシウム、オルト燐酸、ほう酸を混合し、エタノールを加えてよく攪拌したものを、過剰のエタノールをウォーターバス上で蒸散させた後アルミナ坩堝に入れ、10℃/minの速度で電気炉で1300℃まで加温した。この温度で4時間溶融した後、炉内で自然放冷し、白色固形物を得た。この白色組成物をアルミナ製乳鉢とアルミナ製乳棒を用いて1mm角程度に粉砕した後、更にフリッチュ社製遊星ボールミルで20分粉砕して200メッシュ以下の微粉末とし、製造例1～4のセメント粉末を得た。

【0017】

【表1】

	製造例1	製造例2	製造例3	製造例4
CaO	84.00	81.50	88.75	88.75
P <sub>2</sub> O <sub>5</sub>	18.00	18.50	21.25	21.25
B <sub>2</sub> O <sub>3</sub>	20.00	20.00	5.00	5.00
SiO <sub>2</sub>	—	—	7.53	2.50
Al <sub>2</sub> O <sub>3</sub>	—	—	2.53	7.60

\*表示はmol%

【0018】(硬化液の製造例)表2の組成となるように、オルト燐酸、燐酸二水素ナトリウムを水溶液とし、製造例5～8の硬化液を得た。

【0019】

【表2】

	製造例5	製造例6	製造例7	製造例8
オルト燐酸	50	40	35	30
燐酸二水素アンモニウム	10	—	15	15
燐酸水素二アンモニウム	—	10	—	5
蒸留水	40	50	50	50

\*表示は重量%

【0020】

【実施例】以下本発明を実施例により詳細に説明する。

【0021】実施例1. 製造例1のセメント粉末20gと製造例5の硬化液5mlを混合し、1×1×2cmの真鍮製金型に充填した。

【0022】実施例2. 製造例2のセメント粉末20gと製造例6の硬化液5mlを混合し、1×1×2cmの真鍮製金型に充填した。

【0023】実施例3. 製造例3のセメント粉末20gと製造例7の硬化液7.5mlを混合し、1×1×2cmの真鍮製金型に充填した。

【0024】実施例4. 製造例4のセメント粉末20gと製造例8の硬化液10mlを混合し、1×1×2cmの真鍮製金型に充填した。

【0025】硬化時間は金型に充填した混練物に、重さ300g、断面積1mm<sup>2</sup>の針を落とし針痕がつかなくなった時間を硬化時間とした。

【0026】圧縮強度は金型充填2時間後、8時間後に硬化した充填物を取り出し、オリエンテック社製圧縮試験機で測定した。また8時間後に取り出した充填物を、199液体培地に3ヶ月浸漬し、同様に圧縮強度を測定した。

【0027】硬化液と混合する前の粉末及び硬化したセメントを粉砕したものの結晶相の同定及び結晶の定量は日本電子社製X線回折計により測定した。以上の結果を表3に示した。

【0028】

【表3】

	実施例1	実施例2	実施例3	実施例4
硬化時間	2分	4分	5分	7分
2時間後の圧縮強度	280kgf/cm <sup>2</sup>	315kgf/cm <sup>2</sup>	345kgf/cm <sup>2</sup>	320kgf/cm <sup>2</sup>
8時間後の圧縮強度	720kgf/cm <sup>2</sup>	780kgf/cm <sup>2</sup>	680kgf/cm <sup>2</sup>	835kgf/cm <sup>2</sup>
3ヶ月浸漬後の圧縮強度	715kgf/cm <sup>2</sup>	760kgf/cm <sup>2</sup>	820kgf/cm <sup>2</sup>	830kgf/cm <sup>2</sup>
セメント粉末の結晶相	$\beta$ -TCP	$\beta$ -TCP	$\beta$ -TCP	$\beta$ -TCP
セメント粉末中の結晶量	79.8	77.4	67.8	68.3
硬化体の結晶相	$\beta$ -TCP	$\beta$ -TCP	$\beta$ -TCP	$\beta$ -TCP
硬化体中の結晶量	78.8	76.5	68.9	68.2

\*結晶量の定量値は重量%

【0029】表3の結果に示された如く、本発明の生体用セメントは早期に自己凝結硬化し且つ硬化初期から圧縮強度が高い。又疑似生体液に3ヶ月浸漬した後も圧縮強度の低下は認められず安定な圧縮強度を保持している。又、生体に対する親和性の高い $\beta$ -TCPの結晶量も硬化反応後もほとんど変化しないことなどが実証され

た。

【0030】

【発明の効果】本発明によれば、硬化速度が速く、強度が高く且つ生体親和性の高い生体用セメントが提供できる。